REMARKS/ARGUMENTS

The Figure legends to Figures 1, 2 and 3 have been amended so that the sequences recited in each Figure have been assigned SEQ ID NO's.

Claim 112 has been amended so that the claimed vector system is now required to comprise a pair of BAAV inverted terminal repeats and a nucleic acid sequence encoding one of the recited proteins.

New claims 151 and 152 have been submitted. Claim 151 is drawn to a vector system comprising at least one vector comprising a nucleic acid sequence encoding an amino acid sequence at least 97% identical to SEQ ID NO:7, 97 % identical to SEQ ID NO:9, or 99% identical to SEQ ID NO:11, or 95% identical to SEQ ID NO:3 or 5. Support for this claim can be found in previous claim 112, and in the specification, for example, on page 19, lines 14-18. Claim 152 specifies that the nucleic acid sequences be selected from SEQ ID NO:7, 9 or 11. Support for this claim is found in previous claim 112 and claim 124.

Accordingly, applicants submit that no new matter has been entered into the specification.

I. Election/Restriction

The Examiner states claims 112-150 are generic to the different species of capsid proteins recited in claim 112(b), for example, and represented by SEQ ID NO's 7, 9, and 11. The Examiner further states that the species are independent or distinct because they are mutually exclusive amino acid or nucleic acid sequences, and are not obvious variants of each other. Consequently, the Examiner is requesting that applicants elect a single species, or grouping of patently indistinct species, for prosecution on the merits.

Applicants disagree that all of the sequences recited in the claims are unrelated. For example, SEQ ID NO's 7, 9 and 11, relate to BAAV capsid protein VP1, VP2 and VP3, respectively. These proteins are all related in that VP3 is a truncated form of VP2, which is itself a truncated form of VP1. Thus, these proteins are identical in sequence in their overlapping regions. This relationship is illustrated by Exhibit A, which shows an alignment of these SEQ ID NO's. This alignment makes it clear that these three amino acids sequences are from the same protein. Further, SEQ ID NO's 6, 8 and 10 represent nucleic acid sequences encoding the amino acid sequences of SEQ ID NO's 7, 9 and 11, respectively. Thus, because SEQ ID NO's 6-11 are so intimately related, applicants request that all of these sequences be examined together.

Similar reasoning applies to SEQ ID NO's 2-5. SEQ ID NO's 3 and 5, as recited in claim 112, represent the amino acid sequences of two forms of the BAAV Rep protein. Specifically, the amino acid sequence represented by SEQ ID NO:5 is a truncated version of SEQ ID NO:3. Consequently, these two

sequences are identical in their overlapping regions. The relationship between these two proteins is clearly illustrated in Exhibit B, which shows an alignment between SEQ ID NO:3 and SEQ ID NO:5. Further, SEQ ID NO's 2 and 4 represent the coding sequences for SEQ ID NO's 3 and 5, respectively. Thus, SEQ ID NO's 2-5 are all intimately related. Consequently, applicants request that these sequences be rejoined and examined together.

With regard to claims 122, 123, 125 and 141-144, applicants fail to see why the Examiner believes the subject matter of these claims to be drawn to a non-elected invention and thus, has withdrawn these claims. The original Group election was to a claim (claim 66) drawn to a vector system comprising at least one vector comprising a nucleic acid selected from the group consisting of I) a pair of inverted terminal repeats; II) a nucleic acid encoding a BAAV capsid protein; and III) a nucleic acid encoding a BAAV Rep protein. While claim 66 was canceled, the new claims (e.g., claim 112) maintain the limitations of the original claim. New claims 112 and 131 merely place further restrictions on the amino acid structure of the capsid and Rep proteins. Likewise, claims 122, 123, 125 and 141-144 further define the structure of the encoding nucleic acid molecules recited in claims 112 and 131. Thus, applicants request that the Examiner reinstate claims 122, 123, 125 and 141-144 and examine all of the claims together.

II. Sequence Rules

The Examiner has objected to the specification stating that Figures 1-3 contain sequences that are not identified by SEQ ID NO's. The Examiner requests that applicants amend the Figures or the description of the drawings to recite the appropriate SEQ ID NO's.

Applicants have amended the Figure Legends for Figures 1-3 to recite the appropriate SEQ ID NO's.

III. Claim Objections

The Examiner has objected to claims 112 and 131, stating that they recite non-elected subject matter. Specifically, the Examiner states that, as currently worded, the claims do not require either of the elected components of the invention, i.e. parts (a) and (b). The Examiner suggests that if applicants would like to include the subject matter of claim 112, part (c), the claim should be amended so that the conjunction "and" appears between the required components.

Applicants respectfully submit that the Examiner has misinterpreted the subject matter of original claim 66, from which the elected Group was derived. Claim 66 was drawn to a vector system comprising at least one vector comprising a nucleic acid selected from the group consisting of I) a pair of inverted terminal repeats; II) a nucleic acid encoding a BAAV capsid protein; and III) a nucleic acid encoding a

BAAV Rep protein. Thus, the vector could contain any one, or all, of the recited nucleic acid sequences, meaning that no one particular sequence is required as suggested by the Examiner. In view of this, applicants request the Examiner withdraw his objection to the claims.

IV. Rejections under 35 U.S.C.

The Examiner has rejected claims 112-114, 116-118, 126-130 as being anticipated by Chiorini et al. (WO99/61601) Specifically, the Examiner states that Chiorini et al. teaches AAV5 vectors comprising two AAV5 ITRs, which are 95% identical to instant SEQ ID NO;12. In addition, the Examiner states that the limitations of present claims 126-130 are found in claims 1-7 of Chiorini et al.

Claim 112 has been amended to specify that the system comprise a pair of BAAV inverted terminal repeats AND a nucleic acid sequence selected from the group consisting of (i) a nucleic acid sequence encoding a protein comprising an amino acid sequence at least 95% identical to SEQ ID NO:7, SEQ I NO:9 or SEQ ID NO:11; and (ii) a nucleic acid sequence at least 95% identical to SEQ ID NO:3, SEQ ID NO:3 or SEQ ID NO:5. Chiorini et al. does not teach a vector system comprising all of these elements. Thus, claim 112 is not anticipated by Chiorini et al. Further, claims 113, 114, 116-118, and 126-130 all depend from claim 112 and further limit the subject matter recited therein. Consequently, these claims are not anticipated by Chiorini et al.

Applicants have added new claim 151, which is drawn to a vector system comprising a nucleic acid sequence selected from (a) a pair of BAAV ITRs, wherein at least one ITR is at least 96% identical to SEQ ID NO:12. The ITRs disclosed by Chiorini et al. are not at least 96% identical to SEQ ID NO:12. Thus, Chiroini et al. does not anticipate new claim 151.

The Examiner has also rejected claims 112 and 120 as being anticipated by Arbetman et al. (US 7,259,151). Specifically, the Examiner states that Arbetman et al. discloses a protein (SEQ ID NO:26) that is 99% identical to present SEQ ID NO:11.

Claim 112 has been amended to specify that the system comprise a pair of BAAV inverted terminal repeats AND a nucleic acid sequence selected from the group consisting of (i) a nucleic acid sequence encoding a protein comprising an amino acid sequence at least 95% identical to SEQ ID NO:7, SEQ I NO:9 or SEQ ID NO:11; and (ii) a nucleic acid sequence at least 95% identical to SEQ ID NO:3, SEQ ID NO:3 or SEQ ID NO:5. Arbetman et al. does not disclose a system comprising the recited VP protein AND a BAAV ITR. Claim 120 depends from claim 112 and thus is also drawn to a system comprising a BAAV ITR. Consequently, Arbetman et al. does not anticipate claims 112 and 120.

With regard to new claims 151, applicants note that the amino acid sequences recited therein are at least at least 97% identical to SEQ ID NO:7, 97% identical to SEQ ID NO:9, or 99% identical to SEQ ID NO:11. As shown in Exhibits C, D and E, SEQ ID NO:26, disclosed by Arbetmann et al., is 96%, 96%, and 98% identical to present SEQ ID NO's 7, 9 and 11, respectively. Consequently, claim 151 is not anticipated by Arbetmann et al.

In view of the above of the fact that the cited prior art does not teach all of the limitations of the present claims, applicants request withdrawal of the rejection for anticipation.

V. Rejections under 35 USC 112, first paragraph –enablement

The Examiner has rejected claims 112-118, 120, 126-140, and 145-150 for lack of enablement. Specifically, the Examiner states that while the specification is enabling for compositions comprising the BAAV ITR and capsid protein set forth in SEQ ID NO's 12 and 10, respectively, is does not enable other BAAV ITRs, capsid proteins, or variants thereof. More specifically, the Examiner states that while the claims read on a broad genus of ITR and protein sequences, applicants only disclose a single sequence for each vector component. In view of this, the Examiner concludes that excessive trial and error experimentation would be required to identify the necessary BAAV ITR and VP3 derivatives having the claimed properties, since the amino acid or nucleic acid sequences of such molecules could not be predicted from the present disclosure.

In stating his reasoning for rejecting the claims, the Examiner alludes to several factors, including the quantity of experimentation necessary, the amount of guidance present in the disclosure and the predictability of the art. However, Applicants believe the Examiner has incorrectly applied such factors to the facts in the present application. Applicants liken the facts in the present case to those in *Ex Parte Kubin*, (2007 Pat. App. LEXIS 13, 83 U.S.P.Q.2.D (BNA) 1410 (Bd. Pat. App. & Interferences May, 2007). In that case, Appellants had disclosed a single polynucleotide sequence encoding a protein, referred to as NAIL and represented by SEQ ID NO:2, but were claiming polynucleotides encoding proteins at least 80% identical to SEQ ID NO:2. Further, the Appellants in that case did not disclose any variants of SEQ ID NO:2 (or encoding nucleic acid molecules). Nor did Appellants disclose any correlation between the disclosed structure and ability of the protein to bind CD48 (the NAIL ligand). Appellants did, however, disclose methods of making variant sequences, and a method of screening the variants for activity. The Examiner in the case rejected the claims for lack of enablement for reasons nearly identical to those issued in the present Application. However, on appeal the Board of Patent Appeals and Interferences reversed the Examiner's decision. In doing so, the Board stated that while molecular biology was generally an unpredictable art, the level of skill in the field was high. Moreover, because methods of making nucleic acid sequences and screening the resultant proteins for activity was

known in the art, the experimentation required to produce other proteins within the scope of the claims was "well within the abilities of those skilled in the art and thus would have been routine." Thus, the Board held that the disclosure enabled nucleic acid sequence encoding proteins at least 80% identical to SEQ ID NO:2

Applying the facts of *Kubin* to the present rejection, Applicants have disclosed specific ITR and capsid protein sequences (e.g., SEQ ID NO:12 and SEQ ID NO:10) that fall within the scope of the claims. Furthermore, the specification teaches how to make variants of the disclosed sequences, and how to calculate the percent identity between the disclosed sequences, and a variant having a specified percent identity (see, for example, page 19, lines 32-34, through page 21, lines 1-15). In addition, Applicants teach methods of producing viral particles and transducing cells, methods that can be used as assays for determining which variants have the desired activities. As was the case in *Kubin*, the level of skill in the art was high at the time of filing, and the technology for making the claimed variants and screening them for activity was well developed. While Applicants acknowledge that the amount of screening necessary to identify all variants falling within the claims might be considerable, the court in *In re Wands, 858 F.2d (1988)* held that, "...a considerable amount of experimentation is permissible if it is merely routine...". As noted by the Board in *Kubin*, the type of screening necessary in the present application is a routine part of modern molecular biology. Thus, because the screening necessary to identify those proteins falling within the scope of the claims is routine, it cannot be considered to rise to the level of undue experimentation. In view of this, Applicants contend the claims are enabled.

VI. Rejection sunder 35 USC 112, first paragraph – written description

The Examiner has rejected claims 112-118, 120, 126-140, and 145-150 for lack of written description. Specifically, the Examiner states that applicants fail to provide any disclosure of what structural feature(s) of the instantly disclosed ITRs or capsid proteins are responsible for the desired activity. The Examiner further states that it is incumbent on the specification to disclose means for identifying such variants commensurate in scope with the coverage sought by the claims. The Examiner therefore concludes that the scope of the claims is not supported by the disclosure of the specification.

Applicants respectfully disagree that the specification fails to adequately describe the claimed proteins and nucleic acid molecules. It is applicant's position that the use of percent identity to describe the claimed nucleic acid and amino acid sequences, satisfies the written description requirement based on the USPTO's own guidelines. In this regard, applicants point to the USPTO's guidelines for compliance with the written description requirement, Written Description Training Materials, Revision 1, dated March 25, 2008 (hereafter "PTO Training Materials"). In particular, applicants refer the Examiner to hypothetical claim 2 of Example 11B, which recites:

> Claim 2. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y.
> PTO Training Materials, page 40.

Example 11B states that the specification only reduces to practice a single species that encodes SEQ ID NO:2 and has activity Y, the species being SEQ ID NO:1. *Id.* at 41. The specification further discloses one or more protein domains responsible for activity Y and predicts that conservative mutations in the domains will result in a protein with activity Y. *Id.* Based on this disclosure, Example 11B concludes that the "specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 2." *Id.* at 42.

Relating the facts of the PTO Training Materials to the present case, the present specification clearly discloses specific nucleic acid and amino acid sequences for the BAAV ITRs and proteins. These core nucleotide sequences serve as the starting (or reference) point for describing all other members of the family. The specification also clearly describes members of the claimed genus as being at least 70-99% identical to the specifically disclosed sequences (see, for example, page 20, lines 9-12). The specification also describes art-recognized methods for modifying polynucleotide and/or amino acid sequences as well as the production of genetically modified organisms expressing the same. Furthermore, the specification teaches that the claimed molecules are capable of forming replication-competent vectors and viruses, thus providing a testable function for the claimed molecules. Therefore, as exemplified in the PTO Training Materials, the instant specification provides full written description support for the present claims. In view of the above, applicants request the Examiner withdraw his rejection of claims 112-118, 120, 126-140, and 145-150 for lack of written description.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in a condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Applicants do not acquiesce to any objection, rejection, or argument not specifically addressed herein. Rather, the Applicants believe the amendments and arguments contained herein overcome all objections, rejections, or arguments.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (303) 863-9700.

The Commissioner is hereby authorized to charge to deposit account number 19-1970 any fees under 37 CFR § 1.16 and 1.17 that may be required by this paper and to credit any overpayment to that

Account. If any extension of time is required in connection with the filing of this paper and has not been separately requested, such extension is hereby petitioned.

Respectfully submitted,
SHERIDAN ROSS P.C.

Date: 5/11/11

By: 

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Exhibit A. Alignment of SEQ ID NO's 7, 9 and 11 from US 10/581,228

```
SEQ ID NO:7      msfvdhppdw lesigdgfre flgleagppk pkanqqkqdn arglvlpgyk
SEQ ID NO:9      .......... .......... .......... .......... ..........
SEQ ID NO:11     .......... .......... .......... .......... ..........


SEQ ID NO:7      ylgpgngldk gdpvnfadev arehdlsyqk qleagdnpyl kynhadaefq
SEQ ID NO:9      .......... .......... .......... .......... ..........
SEQ ID NO:11     .......... .......... .......... .......... ..........


SEQ ID NO:7      eklasdtsfg gnlgkavfqa kkrileplgl vetpdkTAPA AKKRPLEQSP
SEQ ID NO:9      .......... .......... .......... ......TAPA AKKRPLEQSP
SEQ ID NO:11     .......... .......... .......... .......... ..........


SEQ ID NO:7      QEPDSSSGVG KKGKQPARKR LNFDDEPGAG DGPPPEGPSS GAMSTETEMR
SEQ ID NO:9      QEPDSSSGVG KKGKQPARKR LNFDDEPGAG DGPPPEGPSS GAMSTETEMR
SEQ ID NO:11     .......... .......... .......... .......... ........MR


SEQ ID NO:7      AAAGGNGGDA GQGAEGVGNA SGDWHCDSTW SESHVTTTST RTWVLPTYNN
SEQ ID NO:9      AAAGGNGGDA GQGAEGVGNA SGDWHCDSTW SESHVTTTST RTWVLPTYNN
SEQ ID NO:11     AAAGGNGGDA GQGAEGVGNA SGDWHCDSTW SESHVTTTST RTWVLPTYNN


SEQ ID NO:7      HLYLRLGSSN ASDTFNGFST PWGYFDFNRF HCHFSPRDWQ RLINNHWGLR
SEQ ID NO:9      HLYLRLGSSN ASDTFNGFST PWGYFDFNRF HCHFSPRDWQ RLINNHWGLR
SEQ ID NO:11     HLYLRLGSSN ASDTFNGFST PWGYFDFNRF HCHFSPRDWQ RLINNHWGLR


SEQ ID NO:7      PKSMQVRIFN IQVKEVTTSN GETTVSNNLT STVQIFADST YELPYVMDAG
SEQ ID NO:9      PKSMQVRIFN IQVKEVTTSN GETTVSNNLT STVQIFADST YELPYVMDAG
SEQ ID NO:11     PKSMQVRIFN IQVKEVTTSN GETTVSNNLT STVQIFADST YELPYVMDAG


SEQ ID NO:7      QEGSLPPFPN DVFMVPQYGY CGLVTGGSSQ NQTDRNAFYC LEYFPSQMLR
SEQ ID NO:9      QEGSLPPFPN DVFMVPQYGY CGLVTGGSSQ NQTDRNAFYC LEYFPSQMLR
SEQ ID NO:11     QEGSLPPFPN DVFMVPQYGY CGLVTGGSSQ NQTDRNAFYC LEYFPSQMLR


SEQ ID NO:7      TGNNFEMVYK FENVPFHSMY AHSQSLDRLM NPLLDQYLWE LQSTTSGGTL
SEQ ID NO:9      TGNNFEMVYK FENVPFHSMY AHSQSLDRLM NPLLDQYLWE LQSTTSGGTL
SEQ ID NO:11     TGNNFEMVYK FENVPFHSMY AHSQSLDRLM NPLLDQYLWE LQSTTSGGTL


SEQ ID NO:7      NQGNSATNFA KLTKTNFSGY RKNWLPGPMM KQQRFSKTAS QNYKIPQGRN
SEQ ID NO:9      NQGNSATNFA KLTKTNFSGY RKNWLPGPMM KQQRFSKTAS QNYKIPQGRN
SEQ ID NO:11     NQGNSATNFA KLTKTNFSGY RKNWLPGPMM KQQRFSKTAS QNYKIPQGRN


SEQ ID NO:7      NSLLHYETRT TLDGRWSNFA PGTAMATAAN DATDFSQAQL IFAGPNITGN
SEQ ID NO:9      NSLLHYETRT TLDGRWSNFA PGTAMATAAN DATDFSQAQL IFAGPNITGN
SEQ ID NO:11     NSLLHYETRT TLDGRWSNFA PGTAMATAAN DATDFSQAQL IFAGPNITGN
```

SEQ ID NO:7 TTTDANNLMF TSEDELRATN PRDTDLFGHL ATNQQNATTV PTVDDVDGVG
SEQ ID NO:9 TTTDANNLMF TSEDELRATN PRDTDLFGHL ATNQQNATTV PTVDDVDGVG
SEQ ID NO:11 TTTDANNLMF TSEDELRATN PRDTDLFGHL ATNQQNATTV PTVDDVDGVG

SEQ ID NO:7 VYPGMVWQDR DIYYQGPIWA KIPHTDGHFH PSPLIGGFGL KSPPPQIFIK
SEQ ID NO:9 VYPGMVWQDR DIYYQGPIWA KIPHTDGHFH PSPLIGGFGL KSPPPQIFIK
SEQ ID NO:11 VYPGMVWQDR DIYYQGPIWA KIPHTDGHFH PSPLIGGFGL KSPPPQIFIK

SEQ ID NO:7 NTPVPANPAT TFSPARINSF ITQYSTGQVA VKIEWEIQKE RSKRWNPEVQ
SEQ ID NO:9 NTPVPANPAT TFSPARINSF ITQYSTGQVA VKIEWEIQKE RSKRWNPEVQ
SEQ ID NO:11 NTPVPANPAT TFSPARINSF ITQYSTGQVA VKIEWEIQKE RSKRWNPEVQ

SEQ ID NO:7 FTSNYGAQDS LLWAPDNAGA YKEPRAIGSR YLTNHL
SEQ ID NO:9 FTSNYGAQDS LLWAPDNAGA YKEPRAIGSR YLTNHL
SEQ ID NO:11 FTSNYGAQDS LLWAPDNAGA YKEPRAIGSR YLTNHL

Exhibit B. Alignment of SEQ ID NO's 3 and 5 from US10/581,228

```
SEQ ID NO:3      matfyevivr vpfdveehlp gisdnfvdwv tgqiwelppe sdlnltlieq
SEQ ID NO:5      .......... .......... .......... .......... ..........

SEQ ID NO:3      pqltvadrir rvflyewnkf skqeskffvq fekgseyfhl htlvetsgis
SEQ ID NO:5      .......... .......... .......... .......... ..........

SEQ ID NO:3      smvlgryvsq iraqlvkvvf qnieprindw vaitkvkkgg ankvvdsgyi
SEQ ID NO:5      .......... .......... .......... .......... ..........

SEQ ID NO:3      payllpkvqp elqwawtnle eyklaalnle erkrlvaqfq lessqrsqea
SEQ ID NO:5      .......... .......... .......... .......... ..........

SEQ ID NO:3      ssqrdvsadp viksktsqky MALVSWLVEH GITSEKQWIQ ENQESYLSFN
SEQ ID NO:5      .......... .......... MALVSWLVEH GITSEKQWIQ ENQESYLSFN

SEQ ID NO:3      STGNSRSQIK AALDNASKIM SLTKSASDYL VGQTVPEDIS ENRIWQIFDL
SEQ ID NO:5      STGNSRSQIK AALDNASKIM SLTKSASDYL VGQTVPEDIS ENRIWQIFDL

SEQ ID NO:3      NGYDPAYAGS VLYGWCTRAF GKRNTVWLYG PATTGKTNIA EAISHTVPFY
SEQ ID NO:5      NGYDPAYAGS VLYGWCTRAF GKRNTVWLYG PATTGKTNIA EAISHTVPFY

SEQ ID NO:3      GCVNWTNENF PFNDCVEKML IWWEEGKMTS KVVEPAKAIL GGSRVRVDQK
SEQ ID NO:5      GCVNWTNENF PFNDCVEKML IWWEEGKMTS KVVEPAKAIL GGSRVRVDQK

SEQ ID NO:3      CKSSVQVDST PVIITSNTNM CVVVDGNSTT FEHQQPLEDR MFRFELMRRL
SEQ ID NO:5      CKSSVQVDST PVIITSNTNM CVVVDGNSTT FEHQQPLEDR MFRFELMRRL

SEQ ID NO:3      PPDFGKITKQ EVKDFFAWAK VNQVPVTHEF MVPKKVAGTE RAETSRKRPL
SEQ ID NO:5      PPDFGKITKQ EVKDFFAWAK VNQVPVTHEF MVPKKVAGTE RAETSRKRPL

SEQ ID NO:3      DDVTNTNYKS PEKRARLSVV PETPRSSDVP VEPAPLRPLN WSSRYECRCD
SEQ ID NO:5      DDVTNTNYKS PEKRARLSVV PETPRSSDVP VEPAPLRPLN WSSRYECRCD

SEQ ID NO:3      YHAKFDSVTG ECDECEYLNR GKNGCIFHNA THCQICHAVP PWEKENVSDF
SEQ ID NO:5      YHAKFDSVTG ECDECEYLNR GKNGCIFHNA THCQICHAVP PWEKENVSDF

SEQ ID NO:3      NDFDDCNKEQ
SEQ ID NO:5      NDFDDCNKEQ
```

Exhibit C. Alignment of present SEQ ID NO7: with SEQ ID NO:26 of Arbetman

```
>lcl|45923 SIN26
Length=725

 Score = 1393 bits (3606),  Expect = 0.0, Method: Compositional matrix
adjust.
 Identities = 710/737 (96%), Positives = 710/737 (96%), Gaps = 13/737 (2%)

SIN7        MSFVDHPPDWLESIGDGFREFLGLEAGPPKPKANQQKQDNARGLVLPGYKYLGPGNGLDK  60
            MSFVDHPPDWLESIGD FREFLGLEAGPPKPKANQQKQDNARGLVLPGYKYLGPGNGLDK
SIN26       MSFVDHPPDWLESIGD-FREFLGLEAGPPKPKANQQKQDNARGLVLPGYKYLGPGNGLDK  59

SIN7        GDPVNFADEVAREHDLSYQKQLEAGDNPYLKYNHADAEFQEKLASDTSFGGNLGKAVFQA  120
            GDPVNFADEVAREHDLSYQKQLEAGDNPYLKYNHADAEFQEKLASDTSFGGN GKAVFQA
SIN26       GDPVNFADEVAREHDLSYQKQLEAGDNPYLKYNHADAEFQEKLASDTSFGGN-GKAVFQA  118

SIN7        KKRILEPLGLVETPDKTAPAAKKRPLEQSPQEPDSSSGVGKKGKQPARKRLNFDDEPGAG  180
            KKRILEPL LVETPDKTAPAAKKR LEQSPQEPDSSSGVGKKGKQPARKRLNFDDE GAG
SIN26       KKRILEPL-LVETPDKTAPAAKKR-LEQSPQEPDSSSGVGKKGKQPARKRLNFDDE-GAG  175

SIN7        DGPPPEGPSSGAMSTETEMRAAAGGNGGDAGQGAEGVGNASGDWHCDSTWSESHVTTTST  240
            DGPPPEGPSSGA STETEMRAAAGGNGG          NASGDWHCDSTWSESHVTTTST
SIN26       DGPPPEGPSSGA-STETEMRAAAGGNGGAGQGAEGVG-NASGDWHCDSTWSESHVTTTST  233

SIN7        RTWVLPTYNNHLYLRL-GSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGL  299
            RTWVLPTYNNHLYLRL GSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGL
SIN26       RTWVLPTYNNHLYLRLLGSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGL  293

SIN7        RPKSMQVRIFNIQVKEVTTSNGETTVSNNLTSTVQIFADSTYELPYVMDAGQEGSLPPFP  359
            RPKSM VRIFNIQVKEVTTSNGETTVSNNLTSTV IFADSTYELPYVMDAGQEGSLPPFP
SIN26       RPKSM-VRIFNIQVKEVTTSNGETTVSNNLTSTVHIFADSTYELPYVMDAGQEGSLPPFP  352

SIN7        NDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQMLRTGNNFEMVYKFENVPFHSM  419
            NDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQMLR GNNFEMVYKFENVPF SM
SIN26       NDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQMLR-GNNFEMVYKFENVPF-SM  410

SIN7        YAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSATNFAKLTKTNFSGYRKNWLPGPM  479
            YAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSATNFAKLT  NFSGYRKNWLPGPM
SIN26       YAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSATNFAKLTNKNFSGYRKNWLPGPM  470

SIN7        MKQQRFSKTASQNYKIPQGRNNSLLHYETRTTLDGRWSNFAPGTAMATAANDATDFSQAQ  539
            MKQQRFSKTASQNYKIPQG NNSLLHYETRTTL  RWSNFAPGTAMATAANDATDFSQAQ
SIN26       MKQQRFSKTASQNYKIPQGGNNSLLHYETRTTLR-RWSNFAPGTAMATAANDATDFSQAQ  529

SIN7        LIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLFGHLATNQQNATTVPTVDDVDGV  599
            LIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLFGHLATNQQNATTVPTVDDVDGV
SIN26       LIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLFGHLATNQQNATTVPTVDDVDGV  589

SIN7        GVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPA  659
            GVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPA
SIN26       GVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPA  649

SIN7        TTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNPEVQFTSNYGAQDSLLWAPDNAG  719
            TTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNPEVQFTSN GAQDSLLWAPDNAG
SIN26       TTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNPEVQFTSN-GAQDSLLWAPDNAG  708
```

```
SIN7        AYKEPRAIGSRYLTNHL  736
            AYKEPRAIGSRYLTNHL
SIN26       AYKEPRAIGSRYLTNHL  725
```

Exhibit D. Alignment of present SEQ ID NO:9 and SEQ ID NO:26 of Arbetman

```
>lcl|57337 SIN26
Length=725

 Score = 1132 bits (2929),  Expect = 0.0, Method: Compositional matrix
adjust.
 Identities = 577/601 (96%), Positives = 577/601 (96%), Gaps = 10/601 (2%)

SIN9        TAPAAKKRPLEQSPQEPDSSSGVGKKGKQPARKRLNFDDEPGAGDGPPPEGPSSGAMSTE  60
            TAPAAKKR LEQSPQEPDSSSGVGKKGKQPARKRLNFDDE GAGDGPPPEGPSSGA STE
SIN26       TAPAAKKR-LEQSPQEPDSSSGVGKKGKQPARKRLNFDDE-GAGDGPPPEGPSSGA-STE  190

SIN9        TEMRAAAGGNGGDAGQGAEGVGNASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRL  120
            TEMRAAAGGNGG           NASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRL
SIN26       TEMRAAAGGNGGAGQGAEGVG-NASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRL  249

SIN9        -GSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGLRPKSMQVRIFNIQVKE  179
             GSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGLRPKSM VRIFNIQVKE
SIN26       LGSSNASDTFNGFSTPWGYFDFNRFHCHFSPRDWQRLINNHWGLRPKSM-VRIFNIQVKE  308

SIN9        VTTSNGETTVSNNLTSTVQIFADSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVT  239
            VTTSNGETTVSNNLTSTV IFADSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVT
SIN26       VTTSNGETTVSNNLTSTVHIFADSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVT  368

SIN9        GGSSQNQTDRNAFYCLEYFPSQMLRTGNNFEMVYKFENVPFHSMYAHSQSLDRLMNPLLD  299
            GGSSQNQTDRNAFYCLEYFPSQMLR GNNFEMVYKFENVPF SMYAHSQSLDRLMNPLLD
SIN26       GGSSQNQTDRNAFYCLEYFPSQMLR-GNNFEMVYKFENVPF-SMYAHSQSLDRLMNPLLD  426

SIN9        QYLWELQSTTSGGTLNQGNSATNFAKLTKTNFSGYRKNWLPGPMMKQQRFSKTASQNYKI  359
            QYLWELQSTTSGGTLNQGNSATNFAKLT  NFSGYRKNWLPGPMMKQQRFSKTASQNYKI
SIN26       QYLWELQSTTSGGTLNQGNSATNFAKLTNKNFSGYRKNWLPGPMMKQQRFSKTASQNYKI  486

SIN9        PQGRNNSLLHYETRTTLDGRWSNFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDA  419
            PQG NNSLLHYETRTTL  RWSNFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDA
SIN26       PQGGNNSLLHYETRTTLR-RWSNFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDA  545

SIN9        NNLMFTSEDELRATNPRDTDLPGHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQ  479
            NNLMFTSEDELRATNPRDTDLPGHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQ
SIN26       NNLMFTSEDELRATNPRDTDLPGHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQ  605

SIN9        GPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYS  539
            GPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYS
SIN26       GPIWAKIPHTDGHFHPSPLIGGFGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYS  665

SIN9        TGQVAVKIEWEIQKERSKRWNPEVQFTSNYGAQDSLLWAPDNAGAYKEPRAIGSRYLTNH  599
            TGQVAVKIEWEIQKERSKRWNPEVQFTSN GAQDSLLWAPDNAGAYKEPRAIGSRYLTNH
SIN26       TGQVAVKIEWEIQKERSKRWNPEVQFTSN-GAQDSLLWAPDNAGAYKEPRAIGSRYLTNH  724

SIN9        L  600
            L
SIN26       L  725
```

Exhibit E. Alignment of present SEQ ID NO:11 and SEQ ID NO:11 of Arbetman

```
>lcl|3885 SIN26
Length=725

 Score = 1035 bits (2677),  Expect = 0.0, Method: Compositional matrix
adjust.
 Identities = 508/519 (98%), Positives = 508/519 (98%), Gaps = 6/519 (1%)

SIN11  21   NASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRL-GSSNASDTFNGFSTPWGYFDF  79
            NASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRL GSSNASDTFNGFSTPWGYFDF
SIN26  212  NASGDWHCDSTWSESHVTTTSTRTWVLPTYNNHLYLRLLGSSNASDTFNGFSTPWGYFDF  271

SIN11  80   NRFHCHFSPRDWQRLINNHWGLRPKSMQVRIFNIQVKEVTTSNGETTVSNNLTSTVQIFA  139
            NRFHCHFSPRDWQRLINNHWGLRPKSM VRIFNIQVKEVTTSNGETTVSNNLTSTV IFA
SIN26  272  NRFHCHFSPRDWQRLINNHWGLRPKSM-VRIFNIQVKEVTTSNGETTVSNNLTSTVHIFA  330

SIN11  140  DSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQ  199
            DSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQ
SIN26  331  DSTYELPYVMDAGQEGSLPPFPNDVFMVPQYGYCGLVTGGSSQNQTDRNAFYCLEYFPSQ  390

SIN11  200  MLRTGNNFEMVYKFENVPFHSMYAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSAT  259
            MLR GNNFEMVYKFENVPF SMYAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSAT
SIN26  391  MLR-GNNFEMVYKFENVPF-SMYAHSQSLDRLMNPLLDQYLWELQSTTSGGTLNQGNSAT  448

SIN11  260  NFAKLTKTNFSGYRKNWLPGPMMKQQRFSKTASQNYKIPQGRNNSLLHYETRTTLDGRWS  319
            NFAKLT  NFSGYRKNWLPGPMMKQQRFSKTASQNYKIPQG NNSLLHYETRTTL  RWS
SIN26  449  NFAKLTNKNFSGYRKNWLPGPMMKQQRFSKTASQNYKIPQGGNNSLLHYETRTTLR-RWS  507

SIN11  320  NFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLF  379
            NFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLF
SIN26  508  NFAPGTAMATAANDATDFSQAQLIFAGPNITGNTTTDANNLMFTSEDELRATNPRDTDLF  567

SIN11  380  GHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGG  439
            GHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGG
SIN26  568  GHLATNQQNATTVPTVDDVDGVGVYPGMVWQDRDIYYQGPIWAKIPHTDGHFHPSPLIGG  627

SIN11  440  FGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNP  499
            FGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNP
SIN26  628  FGLKSPPPQIFIKNTPVPANPATTFSPARINSFITQYSTGQVAVKIEWEIQKERSKRWNP  687

SIN11  500  EVQFTSNYGAQDSLLWAPDNAGAYKEPRAIGSRYLTNHL  538
            EVQFTSN GAQDSLLWAPDNAGAYKEPRAIGSRYLTNHL
SIN26  688  EVQFTSN-GAQDSLLWAPDNAGAYKEPRAIGSRYLTNHL  725
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